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CONFIRMED BY SWIFTAIR

Dear Sirs

European Patent Application No. 01 918 824.2-2123
Avocet Polymer Technologies, Inc.
Representative's Ref: 15647/DG

In response to the communication dated 15 June 2004, new pages 32 to 36 are enclosed herewith, to replace former pages 32 to 43. A manuscript amended copy of the former pages is also enclosed, to help the Examiner identify the amendments which have been made.

Amendments

Throughout the claims, the term "healed wound" has been replaced with "closed wound". A basis for this amendment can be found, for example, on page 6 line 16 of the application as filed.

Throughout the claims, the expression "for improving the size and appearance of ..." has been replaced with "for reducing the size and improving the appearance of ...". A basis for this amendment can be found, for example, on page 11 line 27.

Claim 1 now also specifies that the condition is caused by the appearance of a hypertrophic or keloid scar on a wound that is closed after an open wound has been re-epithelialized. A basis for this amendment can be found on page 6 at lines 17 and 18.

Furthermore Claim 1 is now limited to the treatment of wounds selected from the group consisting of: a wound caused by laceration; a wound caused by avulsion; a wound caused by burn; a wound caused by radiation, a wound caused by surgery; a wound caused by chemical facial peel; and a wound caused by accident. A basis for this amendment can be found on page 6 at lines 27 to 28.

In claims 1 and 2 the words "at least one" have been inserted before "cyclooxygenase inhibitor", to more clearly cover the possibility of two or more such materials being present.

Some options have been deleted from claim 2, and the claim has been split into two.

Former claim 3 has been deleted.

In claim 5, the words "at least one" have been inserted before "NF-kB inhibitor", to more clearly cover the possibility of two or more such materials being present.

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Some options have been deleted from claim 7, and the claim has been split into two.

Clarifying amendments have been made to former claims 8 and 9 (new claims 9 and 10).

Former claim 10 has been deleted.

The appendancy of claim 11 has been revised.

Claim 13 has been amended to clarify that the thermal insulating material is used together with at least one cyclooxygenase or NF-kB inhibitor. The final phrase of claim 13 has been deleted as being largely redundant.

The appendancy of claim 14 has been corrected.

The option of "glyceryl monooleate" has been deleted from claim 14.

Former claim 15 has been deleted.

The wording of claim 18 has been clarified.

Former claim 19 has been split into two claims.

Former claims 21 to 23 have been deleted.

The wording of former claim 24 (now claim 21) has been clarified.

Former claim 28 has been split into two claims (new claims 25 and 26).

All amendments are made without prejudice to the possibility of future reinstatement of any excluded matter and/or the subsequent filing of divisional applications based on any matter contained in the application as filed.

Comments

The Examiner argues that the claims lack unity. The Applicant respectfully disagrees. Contrary to the Examiner's view that the claims do not relate to a group of inventions so linked as to form a single general inventive concept, the independent claims of this application are all concerned with the use of non-steroidal anti-inflammatory agents for the treatment of closed wounds.

This general concept is novel. The Examiner relies upon document D1 (EP-A-0146847), but this document does not disclose the treatment of a closed wound. In fact, D1 discloses the use of salicylic acid for preventing the formation of keloids. Specifically, D1 teaches a "preparation for treating burns, which can ensure regeneration by new cells within a short time of that portion of the skin in which the cells have been destroyed by the burn". Thus, D1 teaches a preparation to be applied to open wounds to promote re-epithelialization. In contrast, the present invention teaches the application of an inhibitor to a closed wound to improve the size or appearance of the closed wound after an open wound has been re-epithelialized.

The Examiner alleges that D2 (US-A-4,346,108) teaches that ibuprofen can be used for prevention of scar tissue. The Applicant respectfully disagrees that the teachings of this reference are relevant to the present invention. Specifically, D2 teaches system administration of ibuprofen prior to surgery, whereas the present invention is useful after a wound has closed. Adhesion formation has

some similarities to skin scarring. However, there are many differences. There are many therapies for abdominal adhesions that are not effective for skin scars. Also, skin scarring is different because of the skin bacteria. Internal adhesions are not influenced by bacteria, so the biology is very different.

The Examiner alleges that D3 (DE27 07 537) relates to the use of salicylic acid for the treatment of hypertrophic scars. The Applicant respectfully disagrees that the teachings of this reference are particularly relevant to the present invention. The teaching of Sibley mainly concerns the composition in which the salicylic acid is incorporated. As to its application, such a composition is said to be useful for the local treatment or control of hypertrophic cicatrization in acne. Sibley makes no reference to such treatment either reducing the size of a scar nor of improving its appearance.

Further, D3 clearly is restricted to treatment of acne scarring. As amended herein, Claim 1 of the present application excludes any acne infection or scarring. Moreover, the role of salicylic acid in the composition proposed in D3 is not defined. However, we submit that anyone skilled in the art would expect that a keratolytic agent, such as salicylic, acid would be useful to treat any sort of acne or similar skin infections. Indeed, acne related scarring can not be treated without first stopping the infection. Further, an ongoing acne infection is worsened by acne scarring, which further blocks the drainage of the skin pores. Therefore, D3 correctly teaches that to treat acne skin scarring, one must first improve drainage of hair follicles and sebaceous glands entrapped in the scar. Salicylic acid is standard treatment for acne because it acts to decrease epithelial growth in response to inflammation or infection, thus it opens skin pores, improves drainage of skin pores and drains trapped bacteria. This is common knowledge in dermatology and is described in all dermatology textbooks. In contrast, for burn and trauma related scarring, to which Claim 1 of the present application is directed, there is no need to improve drainage of skin glands and hair follicles. Therefore it is not obvious that salicylic acid would be useful in treating post-burn or other post-trauma scarring. Therein lies the inventive step of the present invention. No one skilled in the art of acne treatment or medicine would expect that salicylic acid would treat or prevent post-trauma skin scars.

The Examiner alleges that D4 (WO-A-98/07425) discloses compounds acting as COX-2 inhibitors (and as TNF inhibitors) for the treatment of keloids or prevention of scar tissue formation. The Applicant respectfully disagrees that the teachings of D4 affect the novelty of the present invention. Specifically, D4 does not teach that application of a COX-2 inhibitor to a closed wound improves the size or appearance of the closed wound. Rather, D4 teaches that TNF plays a role in mediating or exacerbating keloid or scar formation and that application of a compound of "formula 1" can inhibit TNF production. In fact animal models for testing the anti inflammatory activity were chosen that were relatively insensitive to cyclooxygenase inhibitors (page 13, line 19-21).

Although the general concept of the treatment of a closed wound with a non-steroidal anti-inflammatory agent is novel, the Applicant has chosen not to present a broad claim to this concept, but rather to present a number of independent claims to embodiments of the general concept. The Applicant is entitled to make this choice and, we submit, in so doing cannot generate disunity which would not have been present if a single independent generic claims had been presented.

The Examiner is therefore respectfully requested to reconsider the disunity objection.

With reference to document D5, and the Examiner's comments with respect to the relevance thereof to the invention of claim 13 etc., the applicant would draw the Examiner's attention to the amendment made to claim 13 which clarifies that the thermal insulating material is used together with at least one cyclooxygenase on NF-kB inhibitor. Document D5 neither discloses nor suggests

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inhibiting cyclooxygenase activity, directly or indirectly, to achieve improvement in the size or appearance of a closed wound. The Examiner is therefore respectfully requested to reconsider the relevance of document D5.

In view of the extent of the amendments made to the claims, the Applicant would prefer to receive the Examiner's reaction thereto, and to the arguments presented above, before making any consequential amendments which may be necessary to the description.

However, if the Examiner has any further problems, he is invited to contact the undersigned by telephone to discuss the application or arrange an informal interview.

- In the alternative that the Examiner considers that the application does not comply with the requirements of the EPC and the Examiner is minded to reject the application, I hereby request oral proceedings for the Applicants to further present their case.

Yours faithfully

D Gambell

Derek Gambell
Representative for the Applicant

Enc.